

CLAIMS

1. An immunomodulatory product, characterized in that it is obtained according to a method of preparation comprising the following steps:

- inoculation and incubation, under aerobic or anaerobic conditions and at a temperature of between approximately 30 and 40°C, of *Bifidobacterium* comprising at least the strain *Bifidobacterium breve* I-2219 in an aqueous substrate having a pH of between approximately 6 and 8 and comprising at least the following ingredients:

- i) lactoserum permeate,
- ii) a lactoserum protein hydrolyzate,
- iii) lactose,

- removal of the *Bifidobacterium* from the aqueous substrate;

- ultrafiltration of the aqueous substrate through filtration membranes having a cut-off threshold of between 100 and 300 kDa, so as to obtain a concentrated retentate;

- dehydration of the concentrated retentate,
- dissolution of the dehydrated retentate in a buffer;

- gel exclusion chromatography of the retentate solution, on a column having an exclusion threshold of 600 kDa;

- recovery of the excluded fraction at the end of the chromatography, which fraction constitutes the immunomodulatory product.

2. The immunomodulatory product as claimed in claim 1, characterized in that the *Bifidobacterium* bacteria are inoculated into the aqueous substrate in a proportion of 1×10^4 to 4×10^9 colony forming units per ml of substrate.

3. The immunomodulatory product as claimed in claim 1

or 2, characterized in that the temperature of the substrate is maintained at a value of between 37 and 40°C throughout the incubation period.

5 4. The immunomodulatory product as claimed in any one of claims 1 to 3, characterized in that the pH of the aqueous substrate is maintained at a value of between 6 and 8 throughout the incubation period.

10 5. The immunomodulatory product as claimed in claim 4, characterized in that the pH of the aqueous substrate is maintained at a value of between 6.5 and 7.5 throughout the incubation period.

15 6. The immunomodulatory product as claimed in any one of the preceding claims, characterized in that the ingredients of the aqueous substrate are present in the following amounts:

20 i) lactoserum permeate: from 3 to 80 g,
 ii) lactoserum protein hydrolyzate: from 2 to 80 g,
 iii) lactose: from 5 to 50 g,
these amounts being given per liter of said aqueous substrate.

25 7. The immunomodulatory product as claimed in claim 6, characterized in that the ingredients of the aqueous substrate are present in the following amounts:

30 i) lactoserum permeate: from 40 to 60 g,
 ii) lactoserum protein hydrolyzate: from 5 to 15 g,
 iii) lactose: from 10 to 30 g,
these amounts being given per liter of said aqueous substrate.

35 8. The immunomodulatory product as claimed in any one of the preceding claims, characterized in that the aqueous substrate also comprises at least one additional ingredient

chosen from buffer salts, yeast extracts and cysteine hydrochloride.

5 9. The immunomodulatory product as claimed in claim 8, characterized in that the aqueous substrate comprises a buffer salt chosen from sodium dihydrogen phosphate and potassium dihydrogen phosphate, which represents from 0.5 to 5 g per liter of aqueous substrate.

10 10. The immunomodulatory product as claimed in claim 8, characterized in that the yeast extract represents from 0.5 to 5 g per liter of aqueous substrate.

15 11. The immunomodulatory product as claimed in claim 8, characterized in that the cysteine hydrochloride represents from 100 to 500 mg per liter of aqueous substrate.

20 12. The immunomodulatory product as claimed in any one of the preceding claims, characterized in that the removal of the *Bifidobacterium* from the culture medium is carried out by microfiltration or by centrifugation of the aqueous substrate.

25 13. The immunomodulatory product as claimed in claim 12, characterized in that the removal of the *Bifidobacterium* from the culture medium is carried out by centrifugation of the aqueous substrate.

30 14. The immunomodulatory product as claimed in any one of the preceding claims, characterized in that the method also comprises, after the *Bifidobacterium* removal step, an additional step consisting of destruction of the residual enzymatic activities contained in the aqueous substrate after incubation.

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15. The immunomodulatory product as claimed in any one of

the preceding claims, characterized in that the exclusion chromatography is carried out on a crosslinked agarose and dextran gel.

5 16. The immunomodulatory product as claimed in any one of the preceding claims, characterized in that the excluded fraction essentially consists of a complex of polysaccharides and of proteins in which the carbohydrate fraction represents from 5 to 30% by weight, the protein
10 fraction representing from 70 to 95% by weight relative to the total weight of said complex.

15 17. The immunomodulatory product as claimed in claim 16, characterized in that the carbohydrate fraction of the excluded fraction has the following monosaccharide composition (expressed as molar ratios with respect to rhamnose): galactose: 5.5 to 8; mannose: 0.8 to 1.3; glucose: 2.5 to 5; N-acetylgalactosamine: 0.3 to 1; N-acetylglucosamine: 0.07 to 0.3; neuraminic acid: 0 to
20 0.15, and rhamnose: 1.

18. The immunomodulatory product as claimed in claim 16, characterized in that the protein fraction comprises at least one peptide corresponding to at least one of the
25 following sequences:

- RELGIGTPSFLHNGGQWYIYA (SEQ ID No. 1)
- RVLNPGQYXYVR (SEQ ID No. 2)
- EQATANGQVSSGQQSTGGS AAP (SEQ ID No. 3).

30 19. The immunomodulatory product as claimed in any one of the preceding claims, as a medicament.

20. The immunomodulatory product as claimed in any one of the preceding claims, as an immunomodulatory medicament.

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21. A pharmaceutical composition, characterized in that it

contains, as active principle, at least one immunomodulatory product obtained according to the method as defined in any one of claims 1 to 18, and at least one pharmaceutically acceptable carrier.

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22. The pharmaceutical composition as claimed in claim 21, characterized in that it is intended for oral administration and in that it is in the form of a liquid or of a solid.

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23. A food composition, characterized in that it contains, as ingredient, at least one immunomodulatory product obtained according to the method as defined in any one of claims 1 to 18.

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24. The food composition as claimed in claim 23, characterized in that it is in the form of a fermented or non-fermented, milk or non-milk preparation, of animal or plant origin, including infant formulas, or for adults or senior citizens.

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25. The food composition as claimed in claim 24, characterized in that it is in the form of liquid or powdered milk, of fresh products, of cereals, of biscuits (fodder), of jars of baby food, of desserts, of products for hospitals, of dietetic products or of nutritional supplements.

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